REMARKS

Status of the Claims

Pending claims

Claims 1 to 7 as filed are pending.

Claims amended, canceled and added in the instant amendment

Claims 1 to 7 are canceled, without prejudice, and new claims 8 to 65 are added. Thus, after entry of the instant amendment, claims 8 to 65 will be pending.

Outstanding Rejections

Claims 1 to 7 stand rejected under 35 U.S.C. §112, second paragraph. Claims 1 to 7 stand rejected under 35 USC §102(b) as allegedly anticipated by Hacia, et al., (1996) Nature Genetics 14:44107. Applicants respectfully traverse all outstanding objections to the specification and rejections of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for new claims directed to compositions and methods for making and using modified biological molecules, including polypeptides, polysaccharides, lipids, and small molecules, can be found, *inter alia*, on page 8, lines 9 to16; page 14, lines 11 to 20; and Examples 18 and 19, page 19, line 14 to page 21, line 2. Support for new claims directed various array surfaces can be found, *inter alia*, on page 7, lines 25 to 30. Support for new claims directed to compositions comprising a chemical compound having a cyclic or ring ether and an alkoxysilane can be found, inter alia, on page 10, line 25 to page 11, line 5.

Issues under 35 U.S.C. §112, second paragraph

Claims 1 to 7 stand rejected under 35 U.S.C. §112, second paragraph, for being indefinite with regard to the term "high density." The instant amendment addresses the Examiner's concerns.

Issues under 35 U.S.C. §102(b)

Claims 1 to 7 stand rejected under 35 USC §102(b) as allegedly anticipated by Hacia, et al., (1996) Nature Genetics 14:44107 (hereinafter "Hacia").

The Patent Office alleges that Hacia teaches high density arrays comprising 50 micron spots.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

Applicants have canceled pending claims 1 to 7, without prejudice. The new claims are drawn, inter alia, to modified biological molecules comprising a biological molecule covalently bound to a compound having the formula: $R_1 — X — R_2$, wherein R_1 is a ring ether group (e.g., an epoxide group) or an amino group, R_2 is an alkoxysilane group; and wherein X is a moiety chemically suitable for linking the epoxide group and the alkoxysilane group; modified biological molecules comprising a biological molecule covalently bound to a compound having the formula: $—HN—(CH_2)_n—Si(OR)_3$; and, biological molecule covalently bonded to a compound having the formula; modified biological molecules comprising a biological molecule

covalently bound to a compound having the formula: $R_1 — X — R_2$; wherein R_1 is a cyclic ether; wherein R_2 is $—NR_4$, wherein each R_3 group are the same or different alkyl groups, and R_4 is —H or an alkyl group; wherein X is moiety, chemically suitable for linking the cyclic ether group and the alkoxysilane group; arrays comprising these compositions, and, methods for making and using these compositions.

In view of the above remarks, Applicants submit that, after entry of the instant amendment, the pending claimed invention is distinguished and not anticipated by the cited art. Accordingly, the Examiner is respectfully requested to withdraw the rejection under 35 U.S.C. §112, second paragraph, and 35 U.S.C. §102(b).

CONCLUSION

Applicants believe all claims pending in this application after entry of the instant amendment are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If necessary, please apply additional and necessary charges, and apply all credits, to Deposit Account No. 06-1050.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date: July 3, 2001

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Appendix A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicant : Bradley et al. Art Unit : 1656
Serial No. : 09/546,085 Examiner : Scott W. Houtteman
Filed : April 10, 2000
Title : CHEMICALLY MODIFIED BIOLOGICAL MOLECULES AND METHODS FOR COUPLING BIOLOGICAL MOLECULES TO SOLID SUPPORT

In The Claims:

Claims 1 to 7 were canceled, without prejudice

The following new claims have been added:

--8. A modified biological molecule comprising a biological molecule covalently bound to a compound having the formula: $R_1 — X — R_2$, wherein R_1 is a cyclic ether group, R_2 is an alkoxysilane group; and X is a moiety chemically suitable for linking the cyclic ether group and the alkoxysilane group.

9. The modified biological molecule of claim 8, wherein the biological molecule comprises a polypeptide or a peptide.

10. The modified biological molecule of claim 8, wherein the biological molecule comprises a polysaccharide or a saccharide.

11. The modified biological molecule of claim 8, wherein the biological molecule comprises a lipid.

12. The modified biological molecule of claim 8, wherein the biological molecule comprises a small molecule.

13. The modified biological molecule of claim 8, wherein the cyclic ether group comprises an epoxide group.

14. The modified biological molecule of claim 13, wherein the epoxide group comprises an ethylene oxide.

15. The modified biological molecule acid of claim 8, wherein the alkoxysilane is selected from the group consisting of —$Si(OCH_3)_3$, —$Si(OC_2H_5)_3$, —$Si(OCH_3)H_2$, —$SI(OCH_3)(CH_3)_2$, and —$Si(OCH)_3)_2CH_3$.

16. The modified biological molecule of claim 8, wherein the compound is 3-glycidoxypropyltrimethoxysilane.

17. A modified biological molecule comprising a biological molecule covalently bound to a compound having the formula: $R_1 — X — R_2$, wherein R_1 is an amino group, R_2 is an alkoxysilane group; and X is a moiety chemically suitable for linking the amino group and the alkoxysilane group.

18. The modified biological molecule of claim 17, wherein the biological molecule comprises a polypeptide or a peptide.

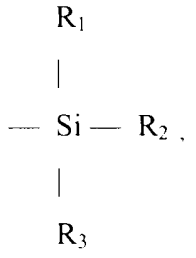
19. The modified biological molecule of claim 17, wherein the biological molecule comprises a polysaccharide or a saccharide.

20. The modified biological molecule of claim 17, wherein the biological molecule comprises a lipid.

21. The modified biological molecule of claim 17, wherein the biological molecule comprises a small molecule.

22. The modified biological molecule of claim 17, wherein the amino group is a primary amine.

23. The modified biological molecule of claim 17 wherein the alkoxysilane is selected from the group consisting of —$Si(OCH_3)_3$, —$Si(OC_2H_5)_3$ and



wherein R_1, R_2 and R_3 are selected from the group consisting of —H, —CH_3, —OCH_3, and —OC_2H_3, and at least one of R_1, R_2 or R_3 is either —OCH_3 or —OC_2H_3.

24. The modified biological molecule of claim 17, wherein the compound is 3-aminopropyltriethoxysilane.

25. A microarray comprising:

a solid support, and

modified biological molecules, as set forth in claim 8 or claim 17, immobilized onto the solid support.

26. The microarray of claim 25, wherein the solid support comprises hydroxyl groups.

27. The microarray of claim 25, wherein the solid support comprises a glass.

28. The microarray of claim 25, wherein the solid support comprises a surface selected from the group consisting of a quartz, a mica, an alumina, a titania, an SnO_2, an RuO_2 and a PtO_2.

29. The microarray of claim 25, wherein the solid support comprises a metal oxide surface.

30. The microarray of claim 25, wherein the solid support comprises a compound selected from the group consisting of a polystyrene, a polyester, a polycarbonate, a polyethylene, a polypropylene, and a nylon.

31. The microarray of claim 25, wherein biological molecules are immobilized onto the solid support in orderly, discrete spots.

32. The microarray of claim 31, wherein the discrete spots are about 50 microns in diameter.

33. A modified biological molecule prepared by a process comprising the steps of:

(a) providing a biological molecule comprising a guanine base or a cytosine base;

(b) reacting the guanine base or the cytosine base with an N-bromosuccinimide at pH about 8.0 to form a brominated biological molecule; and

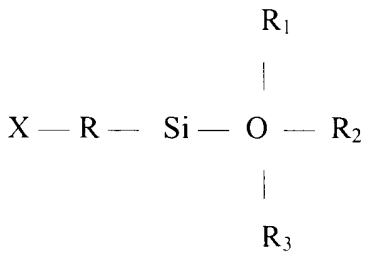
(c) reacting the brominated biological molecule with a silane having the formula —HN— $(CH_2)_n$ —$Si(OR)_3$, wherein n = 3, 4, 5, 6, 7, 8, or 9.

34. The modified biological molecule of claim 33, wherein R is selected from the group consisting of —CH_3, —C_2H_5, and —C_3H_7.

35. A modified biological molecule prepared by a process comprising the steps of:

(a) providing a biological molecule;

(b) providing a compound having a formula



wherein X is a halide and R is a moiety chemically suitable for linking the biological molecule with the Si moiety;

(c) reacting the biological molecule with the compound of step (b) at near neutral pH.

36. The modified biological molecule of claim 35, wherein the halide is selected from the group consisting of a Cl, a Br and an I.

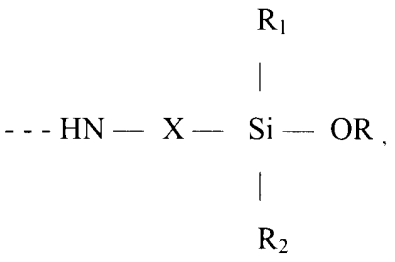
37. The modified biological molecule of claim 35, wherein the R group is selected from the group consisting of a —OCH_3, and a —OC_2H_3.

38. The modified biological molecule of claim 35, wherein the compound of step (b) is selected from the group consisting of 8-bromocytltrichlorosilane, 8-bromocytltrimethoxysilane, 4-chlorobutylmethyldichlorosilane, and 3-iodopropyltrimethoxysilane.

39. A modified biological molecule comprising a biological molecule covalently bound to a compound having the formula: —HN— $(CH_2)_n$ —$Si(OR)_3$, wherein n = 3, 4, 5, 6, 7, 8, or 9.

40. The modified biological molecule of claim 39, wherein R is selected from the group consisting of —CH_3, —C_2H_5, and —C_3H_7.

41. A modified biological molecule comprising a biological molecule covalently bonded to a compound having the formula:



wherein R is selected from the group consisting of —CH_3, —C_2H_5, and —C_3H_7, and R_1 and R_2 are the same or different and are selected from the group consisting of —H, —CH_3, —C_2H_5, —OCH_3, —OC_2H_5, —C_3H_7, and —OC_3H_7; and X is a linking group comprising an at least partially aliphatic chain.

42. A method for immobilizing a biological molecule to a solid support comprising:

reacting a compound of the formula R_1 — X — R_2 with a biological molecule to form a derivatized biological molecule; wherein R_1 is a cyclic ether group; R_2 is an alkoxysilane group; and, X is a moiety chemically suitable for linking the cyclic ether group and the alkoxysilane group; and,

reacting the derivatized biological molecule with the solid support, thereby immobilizing the biological molecule to the solid support.

43. The modified biological molecule of claim 42, wherein the cyclic ether group comprises an epoxide group.

44. The modified biological molecule of claim 43, wherein the epoxide group comprises an ethylene oxide.

45. The method of claim 42 wherein the compound is 3-glycidoxypropyltrimethoxysilane.

46. The method of claim 42, wherein said first reacting step occurs at basic pH.

47. The method of claim 42, wherein said first reacting step occurs at pH from about 6 to about 12.

48. The method of claim 42, wherein said first reacting step occurs at pH from about 6 to about 8.5.

49. The method of claim 42, wherein said pH is greater than 9.5.

50. The method of claim 42, wherein said second reacting step occurs at an approximately neutral pH.

51. A method for immobilizing a biological molecule to a solid support comprising:

reacting a compound of the formula $R_1 — X — R_2$ with a biological molecule to form a derivatized biological molecule, wherein R_1 is an amino group; R_2 is an alkoxysilane group; and, X is a moiety chemically suitable for linking the epoxide group and the alkoxysilane group; and,

reacting the derivatized biological molecule with the solid support, thereby immobilizing the biological molecule to the solid support.

52. The method of claim 51, wherein the compound is 3-aminopropyltriethoxysilane.

53. The method of claim 51, wherein the biological molecule comprises a cytosine residue.

54. The method of claim 51, wherein said first reacting step occurs at essentially neutral pH.

55. The method of claim 51, wherein said first reacting step occurs at a pH of about 6.0 to about 7.0.

56. The method of claim 51, wherein said first reacting step occurs in the presence of sodium bisulfite.

57. The method of claim 42 or 51, wherein said solid support comprises a glass.

58. The method of claim 42 or 51, wherein said biological molecule comprises a DNA or an RNA.

59. The method of claim 42 or 51, wherein the biological molecule comprises a polypeptide or a peptide.

60. The method of claim 42 or 51, wherein the biological molecule comprises a polysaccharide or a saccharide.

61. The method of claim 42 or 51, wherein the biological molecule comprises a lipid.

62. The method of claim 42 or 51, wherein the biological molecule comprises a small molecule.

63. A modified biological molecule comprising a biological molecule covalently bound to a compound having the formula: $R_1 - X - R_2$; wherein R_1 is a cyclic ether; wherein R_2 is $-NR_3$, R_3 is —H or an alkyl group and X is a moiety chemically suitable for linking the cyclic ether group and the alkoxysilane group.

64. A modified biological molecule comprising a biological molecule covalently bonded to a compound having the formula

$$\begin{array}{c} R_1 \\ | \\ -\ Si\ -\ R_2\ , \\ | \\ R_3 \end{array}$$

wherein R_1, R_2 and R_3 are the same or different, and are selected from the group consisting of $-OCH_3$, $-OC_2H_3$, $-OC_2H_7$, and —Cl, and X is a moiety, chemically suitable for linking the biological molecule to the compound.

65. A kit comprising:

a solid support; and,

a device for imprinting an array, wherein the array comprises a modified biological molecule as set forth in claim 8, 17, 33, 35, 39, 41, 63 or 64 onto the solid support.--